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The Reduction of a Natural Diterpene Containing α, β-Unsaturated Keto Group

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Abstract: Hedychenone (**1**), a diterpene containing α, β-unsaturated keto group, was reduced by aluminum-mercury alloy, and a dimerized product (**2)** was obtained as the major product. The coupling occurred at β position of the keto group.

Keywords: Hedychenone, *Hedychium yunnanense,* diterpene, reduction.

Hedychenone(**1**), a labdane-type diterpene, which showed cytotoxic activity against KB cells, was previously isolated from *Hedychium yunnanense*[1]. It was found that the α,β-unsaturated ketone group of **1** showed significant inertness towards some reductants. For example, the $\Delta^{7(8)}$ group of **1** could be reduced by $LiAlH_4$ in THF while the keto group was not affected[2]. Furthermore, both of the $\Delta^{7(8)}$ double bond and C-6 keto group of **1** could not be reduced by $NaBH_4$ in MeOH[3]. In our recent studies, **1** was reduced by aluminum-mercury alloy in refluxed HCl-MeOH solution for 3 hours. After the reaction the alloy residue was removed through filtration and the solution was diluted with water and extracted with EtOAc. The EtOAc extract was subjected to column chromatography over silica gel eluted with petroleum ether-EtOAc (v/v 10:1) to produce a white powder **2** as the major product. On the basis of spectral data, **2** was determined to be an oddly dimerized product of **1**, and the mechanism of the dimmer formation was deduced in **Scheme 1**.

Compound **2** was obtained as white powder. The HREIMS determined the molecular formula of **2** to be $C_{40}H_{58}O_4$., which was almost twice as that of **1**, indicating that **2** was a dimerized product. The ^{13}C NMR spectra of **2** showed only 20 signals, indicating that **2** had a symmetric structure. The IR data showed the presence of a keto group (1703 cm^{-1}) which was not conjugated with carbon-carbon double bond. The assignment of ^{13}C and ^{1}H NMR signals was supported by DEPT, ^{1}H-^{1}H COSY, HMQC and HMBC spectral data. HMQC showed that the two protons at δ 3.04 and δ 2.07 were directly linked to the same carbon (C-7). The ROESY experiment revealed the cross peaks between δ 3.33 (H-9α)

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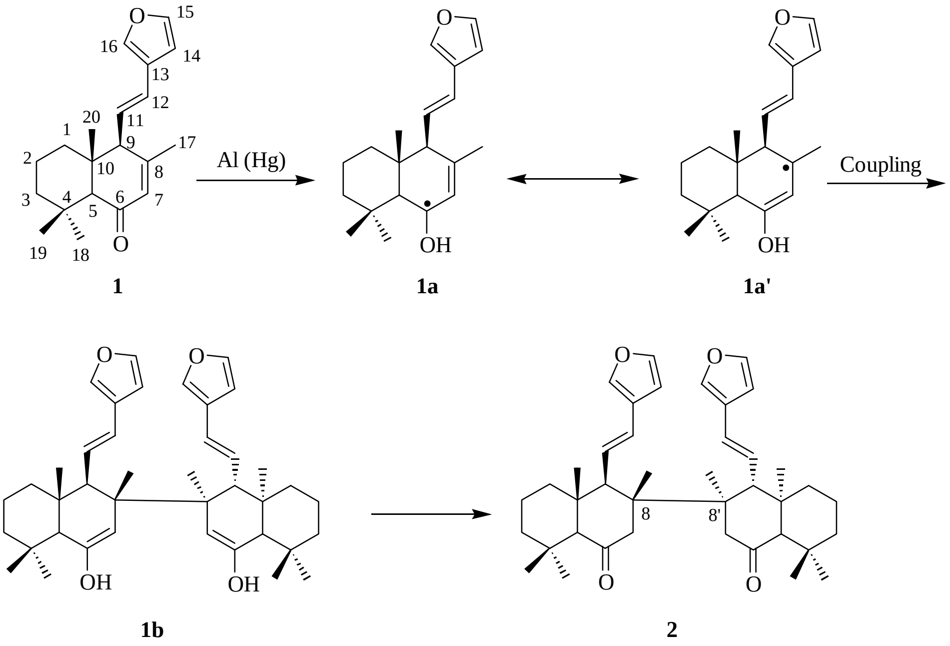
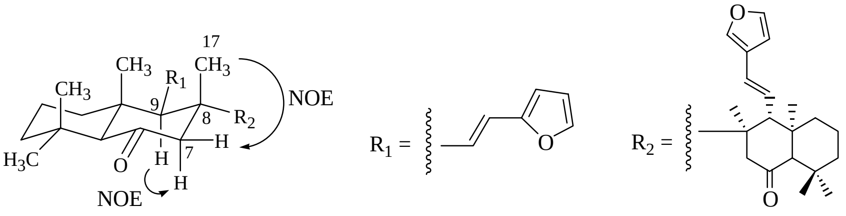
and δ 3.04 (H-7α), and between H-7 β and H-17 (CH_3), indicating the methyl group at C-17 was β-oriented (see **Scheme 2**).

Scheme 1



Scheme 2



The mechanism can be elucidated as follows: at first, **1** was reduced to a radical intermediate **1a**, which had a resonant structure **1a**'. The space hinderance effectively prohibited the coupling occurring at C6 and C6'. Therefore, the coupling at the less hindered positions, C8 and C8', was much more favorable. As a result, **1b** was formed as the major product, which underwent an isomerization process to get the final product **2**.

Table 1 ^{13}C NMR (125MHz) and ^{1}H NMR (500MHz) data of **2** (C_5D_5N, δ, ppm)

No.	^{13}C	^{1}H	No.	^{13}C	^{1}H
1	42.4		11	128.9	6.29 (dd, 10.5, 16.0)
2	18.8		12	125.5	6.84 (d, 16.0)
3	43.0		13	125.2	
4	32.7		14	108.3	6.99 (s)
5	65.8	2.09 (s)	15	141.1	7.69 (s)
6	212.1		16	145.0	8.01 (s)
7	54.0	3.04 (d, 12.2), 2.07 (d, 12.2)	17	18.5	0.91 (s)
8	49.2		18	32.0	0.76 (s)
9	57.7	3.33 (d, 10.5)	19	22.1	1.32 (s)
10	43.6		20	18.4	0.93 (s)

Coupling constants (Hz) in parentheses.

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